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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,782	05/10/2002	Johan Memelink	BO 43339	7997

466 7590 01/04/2007

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/890,782	MEMELINK ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 12, 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *74-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *74-82,84-88* is/are rejected.

7)☒ Claim(s) *83* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *0706*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on October 12, 2006 has been entered.

Claims 1-73 are cancelled.

Claims 74-88 are new.

Claims 74-88 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 74-81, 84-85 and 88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the

claimed invention. This is a new matter rejection. Claims 74 and 75-81 appear to require an AP2-domain transcription factor comprising at least one AP-2 domain having an amino acid sequence with at least 90% amino acid sequence identity with SEQ ID NO:6. An AP-2 domain having an amino acid sequence with at least 90% amino acid sequence identity with SEQ ID NO:6 does not find support in the specification as filed, and thus constitutes new matter. Claims 84, 85 and 88 require an AP2 transcription factor wherein the AP2-domain comprises SEQ ID NO:6. An AP2 transcription factor wherein the AP2-domain comprises SEQ ID NO:6 does not find support in the specification as filed, and thus constitutes new matter.

Claims 74-82, 84-85 and 87-88 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record. This is a written description rejection.

Applicants' arguments filed October 12, 2006 have been fully considered but they are not persuasive.

Applicant points out that the previously rejected claims have been cancelled, and that all of the newly added claims are directed to *Catharanthus* plant cells, which cells are a well characterized genus (reply page 7). Applicant also maintains that the prior office action does not provide any evidence as to why one skilled in the art would not be in possession of this genus at the time of filing (reply pages 7-8). Applicant points in particular to *In re Marzocchi* as holding that the description as filed is presumed to be adequate unless evidence or reasoning to the

contrary has been presented (reply page 8). Applicant also maintains that the claims are not directed to undisclosed and uncharacterized sequences obtained from any source as previously asserted, as the new claims require at least 90% identity with SEQ ID NO:6, and beginning at page 11 the specification describes in detail the structural and functional properties of the AP2-domain (reply page 8).

With respect to the newly added claims being directed to *Catharanthus* plant cells, which cells, the Examiner notes that the outstanding rejection is predicated on a lack of descriptive support for the genus of sequences introduced into the cells, rather than a lack of descriptive support for the genus of cells into which sequences are introduced.

With respect to *In re Marzocchi* , the Examiner maintains that the holding in *In re Marzocchi* is inapposite to the outstanding rejection, which was made under 35 USC 112, first paragraph, for a lack of written description. The holding that Applicants make reference to from *In re Marzocchi* was directed to a rejection which was made under 35 USC 112, first paragraph, for a lack of enablement, which is a separate and distinct section of the statute. Further, an enabling disclosure does not necessarily support the description of a genus of sequences that is not known in the art or disclosed in the specification. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), which discusses the description of a claimed human cDNA sequence based on the disclosure of a rat cDNA sequence and a method for obtaining the human cDNA sequence:

> The patent describes a method of obtaining this cDNA by means of a constructive example, Example 6. This example, however, provides only a general method for obtaining the human cDNA (it incorporates by reference the method used to obtain the rat cDNA) along with the amino acid sequences of human insulin A and B chains. Whether or not it provides an enabling disclosure, it does not provide a written description of the cDNA encoding human insulin, which is necessary to provide a

> written description of the subject matter of claim 5. The name cDNA is not itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA. Describing a method of preparing a cDNA or even describing the protein that the cDNA encodes, as the example does, does not necessarily describe the cDNA itself. (*Lilly*, 43 USPQ2d at 1405)

With respect to possession, the Examiner maintains that possession alone is not sufficient to satisfy the written description requirement for a genus of sequences that is not known in the art or disclosed in the specification.

> See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1617:
>
> Application of the written description requirement, however, is not subsumed by the "possession" inquiry. A showing of "possession" is ancillary to the *statutory* mandate that "[t]he specification shall contain a written description of the invention," and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention. After all, as indicated above, one can show possession of an invention by means of an affidavit or declaration during prosecution, as one does in an interference or when one files an affidavit under 37 C.F.R. § 1.131 to antedate a reference. However, such a showing of possession alone does not cure the lack of a written description in the specification, as required by statute.

The Examiner also maintains that the claims are directed to the use of undisclosed and uncharacterized sequences obtained from any source, as SEQ ID NO: 6 consists of 203 amino acids, which allows for up to any 20 amino acids in the sequence to be substituted by any of 19 alternative amino acids. In this regard it is also noted that the prior art is silent with respect to such sequences, and the specification discloses only a single species encompassed by the claimed genus, a polynucleotide sequence (SEQ ID NO:3) obtained from *Catharanthus roseus* which encodes a single AP2-domain transcription factor (SEQ ID NO:6) that comprises a single Ap2 domain.

Further, the specification beginning at page 11 does not describe the amino acid sequences of AP2-domain transcription factor proteins having at least 90% amino acid identity with SEQ ID NO:6 that function to modulate in catharanthus plant cells the level(s) of one or more terpenoidindole alkaloids and/or the expression of one or more nucleic acids responsible for the biosynthesis of a TIA or a precursor thereof. The specification beginning at page 11 describes only what was known in the art at the time of filing about members of the broader genus of AP2-domain transcription factor proteins. In this regard it is also noted that AP-2 domain transcription factor proteins comprising at least one AP2-domain having at least 90% amino acid identity with SEQ ID NO:6 that function to modulate in catharanthus plant cells the level(s) of one or more terpenoidindole alkaloids and/or the expression of one or more nucleic acids responsible for the biosynthesis of a TIA or a precursor thereof were not known in the art at the time of filing.

Claims 74-82 and 84-88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleotide sequence encoding SEQ ID NO:6, for nucleotide sequences encoding the truncations of SEQ ID NO:6 that are disclosed as Δ5ORCA3 and Δ3ORCA3, and for methods of transforming *Catharanthus roseus* cells with said nucleotide sequences operably linked to a promoter in a sense orientation, does not reasonably provide enablement for nucleotide sequences encoding variants of SEQ ID NO:6, or for other methods of using nucleotide sequences encoding SEQ ID NO:6 or truncations or variants thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record.

Applicant's arguments filed October 12, 2006 have been fully considered but they are not persuasive.

Applicant points out that the previously rejected claims have been cancelled, and that all of the newly added claims are directed to *Catharanthus* plant cells, and to the expression of AP-2 domain transcription factor proteins comprising at least one AP2-domain having at least 90% amino acid identity with SEQ ID NO:6. With respect to the previously cited reference of Memelink et al., Applicant also points out that the claims are not limited to increasing a specific TIA, but rather are directed to modulating TIA levels in plant cells, and that a decrease in a specific TIA can also be desirable. Applicant additionally points out that limiting unwanted TIAs is often accompanied by an increase in a TIA of interest. Applicant maintains that one of ordinary skill in the art could accordingly practice the invention as claimed. (reply page 9)

The Examiner maintains that the full scope of the claimed invention is not enabled, for reasons of record. With respect to modulating TIA levels in plant cells. i.e. increasing or decreasing the levels of particular TIAs, the Examiner maintains that the specification does not provide sufficient guidance with respect to how to use SEQ ID NO:6 or variants thereof to modulate the level of TIAs and precursors and/or intermediates therefore, as the specification does not disclose how to use ORCA-3 (SEQ ID NO:6) or variants thereof to increase or decrease the level of TIAs and precursors and/or intermediates therefore, other than tryptophan and trytptamine, or how to use ORCA-3 to modulate the level of tryptophan and trytptamine other than by increasing their levels. Such guidance is necessary because the effect of expressing SEQ

ID NO:6 or variants thereof on the level of TIAs and precursors and/or intermediates therefore is unpredictable, as the induction of a subset of genes encoding some of the enzymes required for TIA metabolism may or may not result in an increase or decrease in the level of any particular TIAs and precursors and/or intermediates therefore.

See, for example, Memelink J. et al. (ORCAnization of jasmonate-responsive gene expression in alkaloid metabolism. Trends Plant Sci. 2001 May;6(5):212-9. Review), who teach that while *Catharanthus roseus* cells transgenic for and overexpressing ORCA3 (the AP2-domain transcription factor of SEQ ID NO:6) accumulate significant amounts of tryptophan and trytptamine, no TIAs are detected in these cultures (page 216 column 2 last paragraph).

Absent guidance with respect to how to use SEQ ID NO:6 or variants thereof to modulate in a particular manner the level of TIAs and precursors and/or intermediates therefore, one skilled in the art would have to express SEQ ID NO:6 or variants thereof in catharanthus cells under a variety of different conditions in order to determine the specific conditions, if any, under which the level of TIAs and precursors and/or intermediates therefore could be modulated. Such a trial and error to practicing the claimed invention would constitute undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 74, and claims 75-81 dependent thereon, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 74 is indefinite in the recitation of "having an amino acid sequence with at least 90% amino acid sequence identity with SEQ ID

NO:6" It is unclear what object has an amino acid sequence with at least 90% amino acid sequence identity with SEQ ID NO:6, the AP-2 domain transcription factor, or the AP2-domain itself.

Claims 84, 85 and 88 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 84, 85 and 88 are indefinite in the recitation of "wherein the AP2-domain comprises SEQ ID NO:6". It is unclear how the AP-2 domain of the AP2 transcription factor can comprise SEQ ID NO:6, as SEQ ID NO:6 is a full-length AP2 transcription factor, rather than a domain of an AP2 transcription factor.

Claims 74-75 and 77-81 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. Claims 74-75 and 77-81 require providing a catharanthus plant cell, by expression of an AP2-domain encoding nucleotide sequence under the control of an expression regulating sequence, an AP2-domain transcription factor comprising at least one AP2-domain having an amino acid sequence with at least 90% amino acid identity with SEQ ID NO:6, but recite no steps by which this may be accomplished.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 74-75 and 78-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Aerts R.J. et al. (Methyl jasmonate vapor increases the developmentally controlled synthesis of alkaloids in *Catharanthus* and *Cinchona* seedlings. The Plant Journal, Volume 5, Issue 5, May 1994, Pages 635-643).

The claims are drawn to a method comprising providing a *Catharanthus roseus* plant cell, by expression of an AP2-domain encoding nucleotide sequence under the control of an expression regulating sequence, an AP2-domain transcription factor comprising at least one AP2-domain having an amino acid sequence with at least 90% amino acid identity with SEQ ID NO:6.

Aerts R.J. et al. teach a method comprising treating a *Catharanthus roseus* plant cell with methyl jasmonate (page 637 Figures 2 and 3; page 638 Figures 4 and 5; page 640 Figure 7).

While Aerts R.J. et al. are silent with respect to whether their treatment also provides a *Catharanthus roseus* plant cell, by expression of an AP2-domain encoding nucleotide sequence under the control of an expression regulating sequence, an AP2-domain transcription factor comprising at least one AP2-domain having an amino acid sequence with at least 90% amino acid identity with SEQ ID NO:6, the method taught by Aerts R.J. et al. inherently provides a *Catharanthus roseus* plant cell, by expression of an AP2-domain encoding nucleotide sequence under the control of an expression regulating sequence, an AP2-domain transcription factor comprising at least one AP2-domain having an amino acid sequence with at least 90% amino acid identity with SEQ ID NO:6, because the method taught by Aerts R.J. et al. inherently

induces the expression of an AP2-domain transcription factor having an amino acid sequence of SEQ ID NO:6 under the control of its native expression regulating sequence, as evidenced by van der Fits et al. (ORCA3, a jasmonate-responsive transcriptional regulator of plant primary and secondary metabolism. Science. 2000 Jul 14;289(5477):295-7), who teach that methyl jasmonate treatment of *Catharanthus roseus* plant cells induces the expression of the native gene encoding the AP2-domain transcription factor ORCA-3, which has an amino acid sequence of SEQ ID NO:6. (page 296 Fig. 3C).

In this regard it is also noted that Aerts R.J. et al. need not explicitly recognize or teach this inherent end result (provide a *Catharanthus roseus* plant cell, by expression of an AP2-domain encoding nucleotide sequence under the control of an expression regulating sequence, an AP2-domain transcription factor comprising at least one AP2-domain having an amino acid sequence with at least 90% amino acid identity with SEQ ID NO:6) in order to anticipate the claimed invention. See *ex parte Novitski*, 26 USPQ2d 1389 (Bd. Pat. App. & Inter. 1993), in which the Board rejected claims directed to a method for protecting a plant from pathogenic nematodes by inoculating the plant with *Pseudomonas cepacia* type Wisconsin 526 bacteria under 35 USC 102 as being anticipated by Dart et al., whose U.S. patent disclosed a method for protecting a plant from fungal disease by inoculating the plant with *Pseudomonas cepacia* type Wisconsin 526 bacteria. Although Dart et al. was silent with respect to nematode inhibition, the Board concluded that Dart et al. anticipated the rejected claims because nematode inhibition was an inherent property of the bacteria.

Allowable Subject Matter

Claim 83 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form.

Remarks

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins
12/20/06